Table S1. Distribution of MSC and EC in normal and both childhood and adult BCP-ALL bone marrow (BM) according to the BM MRD status at day +15, day +33, and day +78 after starting therapy.

Samples		% BM Stromal Cells From BM Cells	% Mesenchymal Cells From BM Stromal Cells	% Endothelial Cells From BM Stromal Cells	% Blast Cells
Normal/Reactive Donors					
Children (n = 10)		0.064 (0.014–0.087)	80 (71–96)	20 (4–29)	**-**
Adults (n = 6)		0.014 (0.005–0.037)	81 (75–90)	20 (10–25)	**-**
p- value *		**0.011**	0.875	0.875	**-**
BCP-ALL					
Day +15 after therapy					
Children	MRD$^+$ (n = 281 $^\triangle$, n = 226 $^\blacktriangledown$)	0.028 (0–1.57)	77 (13–99)	23 (1–87)	0.620 (0.0002–84)
	MRD$^-$ (n = 28 $^\triangle$, n = 21$^\blacktriangledown$)	0.032 (0–0.40)	74 (30–93)	26 (7–70)	0
p-value *		0.929	0.437	0.436	**<0.001**
Adults	MRD$^+$ (n= 37$^\triangle$, n = 32$^\blacktriangledown$)	0.030 (0–0.95)	73 (15–100)	27 (0–85)	2.000 (0.01–91)
	MRD$^-$ (n = 4 $^\triangle$, n = 3 $^\blacktriangledown$)	0.330 (0–0.57)	94 (77–96)	6 (4–23)	0
p-value *		0.146	0.125	0.125	**<0.001**
Day +33 after therapy					
Children	MRD$^+$ (n= 164 $^\triangle$, n = 158 $^\blacktriangledown$)	0.051 (0–1.85)	76 (49–98)	24 (2–51)	0.018 (0.0002–56)
	MRD$^-$ (n = 118 $^\triangle$, n = 108 $^\blacktriangledown$)	0.045 (0–1.52)	76 (38–97)	24 (3–62)	0
p-value *		0.417	0.226	0.229	**<0.001**
Adults	MRD$^+$ (n = 33 $^\triangle$, n = 29 $^\blacktriangledown$)	0.039 (0–0.3)	67 (0–94)	33 (6–100)	0.050 (0.002–69)
	MRD$^-$ (n = 33 $^\triangle$, n = 28 $^\blacktriangledown$)	0.020 (0–1.11)	76 (28–100)	24 (0–72)	0
p-value *		0.546	0.076	0.076	**<0.001**
Day +78 after therapy					
Children	MRD$^+$ (n = 25 $^\triangle$, n= 25 $^\blacktriangledown$)	0.120 (0.005–0.83)	76 (40–95)	24 (5–60)	0.021 (0.0006–11)
	MRD$^-$ (n = 208$^\triangle$, n = 203 $^\blacktriangledown$)	0.061 (0–1.22)	76 (51–94)	24 (6–49)	0
p- value*		0.351	0.110	0.110	**<0.001**
Adults	MRD+ (n = 16 $^\triangle$, n = 15 $^\blacktriangledown$)	0.024 (0–0.63)	76 (38–98)	24 (2–62)	0.054 (0.0015–63)
	MRD$^-$ (n = 28 $^\triangle$, n = 27 $^\blacktriangledown$)	0.050 (0–0.4)	76 (48–96)	24 (4–52)	0
p-value *		0.583	0.733	0.733	**<0.001**

Abbreviations: BM: bone marrow; BCP-ALL: B-cell precursor acute lymphoblastic leukemia; ND: not detected; $^\triangle$Total number of samples analyzed; $^\blacktriangledown$Number of samples in which stromal cells were present; * Kruskal–Wallis test.

Table S2. Univariate and multivariate analysis of prognostic factors for disease-free survival (DFS) of patients included in the discovery cohort of childhood BCP-ALL (n = 116).

		Univariate Analysis			Multivariate Analysis		
	Median DFS (Years)	HR	95th CI	*p*-Value	HR	95th CI	*p*-Value
Age at diagnosis ≥ 1 to <10 years	5.60	1					
<1 or ≥ 10 years	4.67	2.62	(1.14–6.03)	**0.024**			
Gender Female	5.27	1					
Male	5.63	1.34	(0.64–3.22)	0.383			
WBC at diagnosis $\leq 50 \times 10^9$/L	5.88	1					
>50×10^9/L	4.69	1.45	(0.54–3.87)	0.461			
PB Blasts at Day +8 $< 1 \times 10^9$/L	5.95	1					
$\geq 1 \times 10^9$/L	4.45	1.40	(0.90–2.16)	0.134			
Genetic Abnormalities Favorable	5.95	1					
Adverse	3.01	3.30	(1.02–10.65)	**0.046**			
Follow-up MRD:							
Day +15 MRD⁻	ND *	1					
MRD⁺	5.76	23.21	(0.04–13.355)	0.332			
Day +33 MRD⁻	5.88	1					
MRD⁺	5.40	2.62	(1.04–6.60)	**0.041**			
Day +78 MRD⁻	5.92	1			1		
MRD⁺	3.30	3.32	(1.13–9.73)	**0.029**	3.28	(1.12–9.66)	**0.031**
% Stromal cells:							
Day +15 $\leq 0.21\%$	5.78	1					
>0.21%	ND *	0.44	(0–51.9)	0.387			
Day +33 $\leq 0.21\%$	6.02	1					
>0.21%	3.85	3.04	(1.20–7.70)	**0.019**			
	5.92	1					

Day +78

≤ 0.21%							
>0.21%	4.52	1.96	(0.79–4.90)	0.150			

% Mesenchymal cells:

Day +15							
≤ 73%	5.53	1					
>73%	5.71	0.49	(0.21–1.17)	1.060			
Day +33	4.81	1					
≤ 73%							
>73%	6.13	0.56	(0.25–1.25)	0.555			
Day +78	4.99	1					
≤ 73%							
>73%	6.06	0.55	(0.26–1.20)	0.134			

% Endothelial cells (EC):

Day +15							
EC ≤ 32%	5.53	1					
EC > 32%	5.44	1.71	(0.72–4.06)	0.226			
Day +33	5.93	1					
EC ≤ 32%							
EC > 32%	5.00	1.27	(0.53–3.07)	0.593			
Day +78	6.01	1			1		
EC ≤ 32%							
EC > 32%	3.97	2.27	(1.01–5.10)	**0.048**	2.50	(1–9.66)	**0.05**

MRD Status and % EC at Day +78:

MRD[-] and EC ≤ 32%	6.09	1					
MRD[+] or EC ≤ 32% MRD[-] or EC > 32%	4.13	2.12	(0.92–4.86)	**0.001**			
MRD[+] and EC > 32%	1.56	9.63	(2.14–43.32)				

CI: confidence interval; HR: hazard ratio; ND: not determined; MRD: minimal residual disease * there were no events in this group.
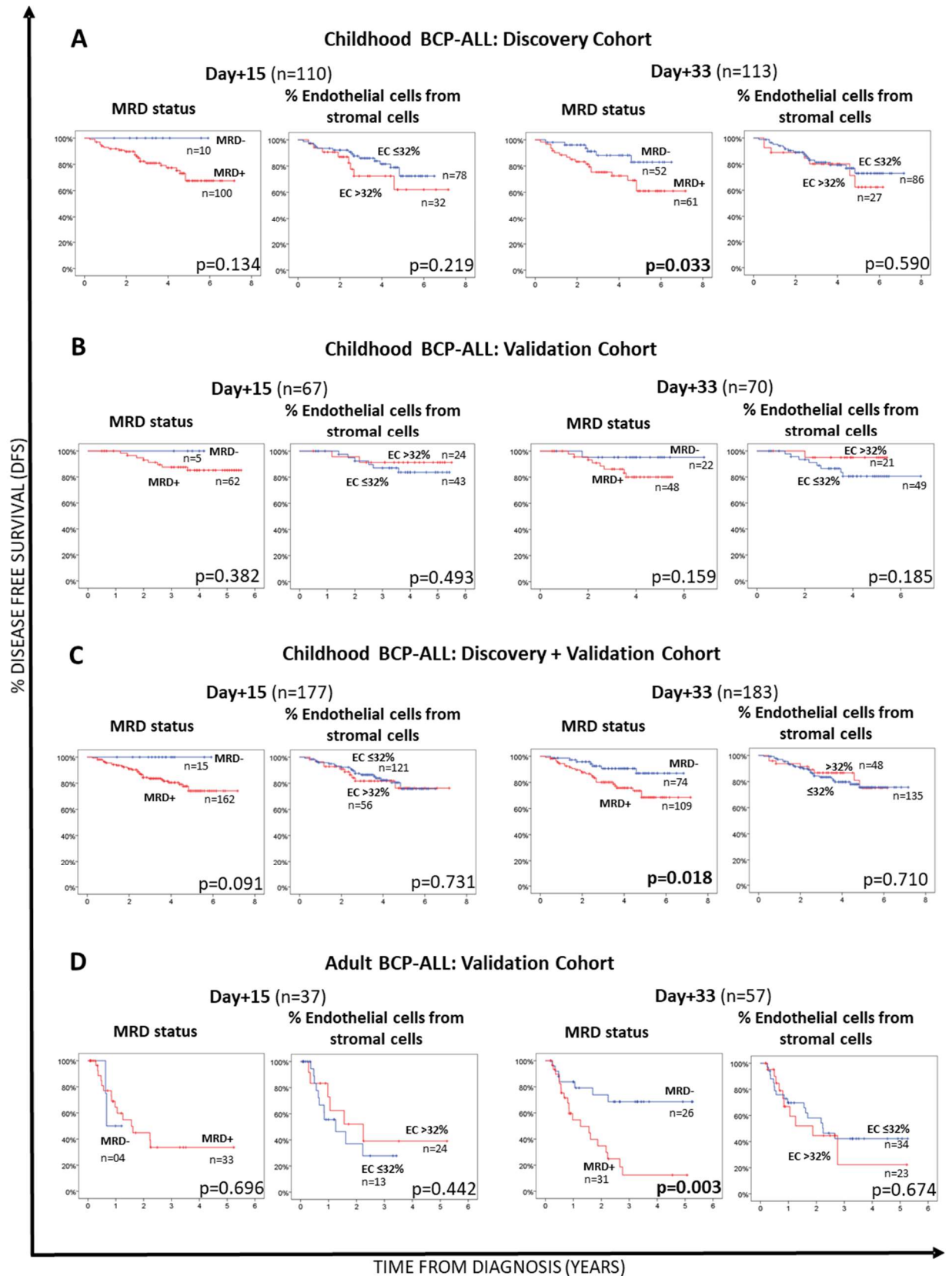
Figure S1. Impact of the BM MRD status and the percentage of BM endothelial cells within the whole BM stromal cell compartment Panels (**A–C**) at day +15 and day +33 of therapy on disease free survival (DFS) of childhood BCP-ALL Panel. (**A**) Discovery cohort; (**B**) validation cohort; (**C**) discovery plus validation cohort); adult BCP-ALL Panel (**D**), respectively. Statistical significance was set at *p* < 0.05 (log-rank test).

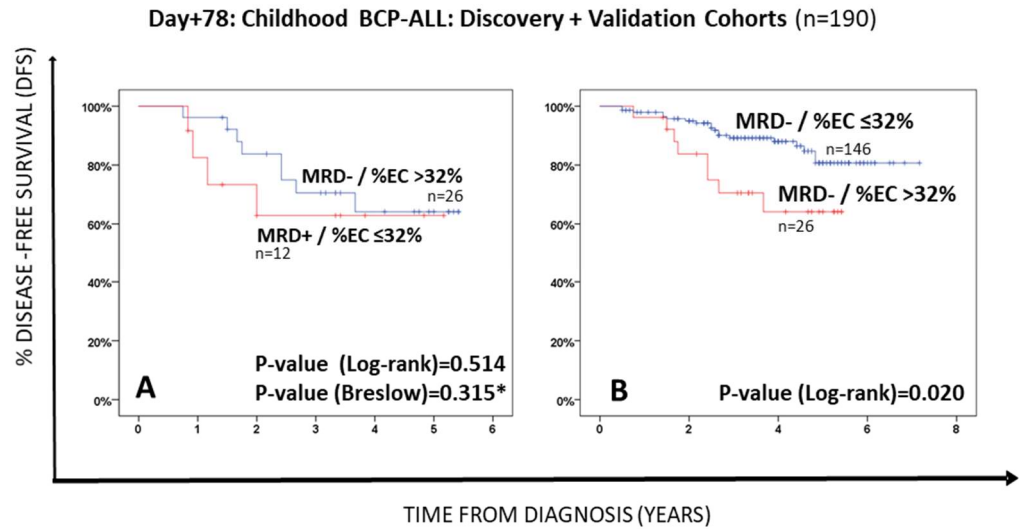**Day+78: Childhood BCP-ALL: Discovery + Validation Cohorts (n=190)**

Figure S2. Impact of the bone marrow (BM) minimal residual disease (MRD) status and the percentage of BM endothelial cells (EC) within the whole BM stromal cell compartment at day +78 of therapy on disease-free survival (DFS) of childhood BCP-ALL for both the discovery plus validation cohorts: comparison between MRD[-] patients with >32% EC in BM vs. MRD[+] cases with ≤32% EC Panel (**A**), and among MRD[-] patients between cases with low (≤32%) vs high (>32%) percentages of EC within BM stromal cells Panel (**B**). Statistical significance was set at $p < 0.05$ (log-rank test). * Breslow test was used in Panel A to exclude a possible statically significant difference at the first part of the curve.